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<120> ACTIVATING MUTATIONS OF PLATELET DERIVED GROWTH FACTOR RECEPTOR
ALPHA (PDGFRA) AS DIAGNOSTIC MARKERS AND THERAPEUTIC TARGETS

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<160> 27

<170> PatentIn version 3.2

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Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
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Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
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Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
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Leu Tyr Thr Cys Tyr  Asn His Thr Gln Thr Glu Glu Asn  Leu
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Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
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Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
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Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
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Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
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Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
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Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ile Met His Asp Ser Asn
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Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
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Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
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Asn	Leu	His	Glu	Val		His	Phe	Val	Val	Glu	Val	Arg	Ala		Pro		
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770 775 780

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Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu

Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
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Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
85 90 95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
100 105 110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
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Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
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Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
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180 185 190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
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290

295

300

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 690 695 700

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775

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 Arg Leu Ser Ala Asp Ser Gly Tyr Ile Ile Pro Leu Pro Asp Ile
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 Asp Pro Val Pro Glu Glu Glu Asp Leu Gly Lys Arg Asn Arg His
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Gln Leu Asn Ser Ser Phe Ser Leu Arg Cys Phe Gly Glu Ser Glu Val	
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Ser Trp Gln Tyr Pro Met Ser Glu Glu Glu Ser Ser Asp Val Glu Ile	
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Arg Asn Glu Glu Asn Asn Ser Gly Leu Phe Val Thr Val Leu Glu Val	
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Ser Ser Ala Ser Ala Ala His Thr Gly Leu Tyr Thr Cys Tyr Tyr Asn	
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His Thr Gln Thr Glu Glu Asn Glu Leu Glu Gly Arg His Ile Tyr Ile	
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Tyr Leu Val Ile Val Glu Asp Asp Asp Ser Ala Ile Ile Pro Cys Arg	
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Val Gly Pro Tyr Ile Cys Glu Ala Thr Val Lys Gly Lys Lys Phe Gln	
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Thr Ile Pro Phe Asn Val Tyr Ala Leu Lys Ala Thr Ser Glu Leu Asp	
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Leu Glu Met Glu Ala Leu Lys Thr Val Tyr Lys Ser Gly Glu Thr Ile	
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Thr Tyr Pro Gly Glu Val Lys Gly Lys Gly Ile Thr Met Leu Glu Glu	
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Ile Lys Val Pro Ser Ile Lys Leu Val Tyr Thr Leu Thr Val Pro Glu	
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Ala Thr Val Lys Asp Ser Gly Asp Tyr Glu Cys Ala Ala Arg Gln Ala	
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Lys Gly Phe Ile Glu Ile Lys Pro Thr Phe Ser Gln Leu Glu Ala Val	
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Asn Leu His Glu Val Lys His Phe Val Val Glu Val Arg Ala Tyr Pro	
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Pro Pro Arg Ile Ser Trp Leu Lys Asn Asn Leu Thr Leu Ile Glu Asn	
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Leu Thr Glu Ile Thr Thr Asp Val Glu Lys Ile Gln Glu Ile Arg Tyr	
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Arg Ser Lys Leu Lys Leu Ile Arg Ala Lys Glu Glu Asp Ser Gly His	
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Glu Leu Leu Thr Gln Val Pro Ser Ser Ile Leu Asp Leu Val Asp Asp	
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His His Gly Ser Thr Gly Gly Gln Thr Val Arg Cys Thr Ala Glu Gly	
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Cys Asn Asn Glu Thr Ser Trp Thr Ile Leu Ala Asn Asn Val Ser Asn	
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Val Thr Phe Ala Lys Val Glu Glu Thr Ile Ala Val Arg Cys Leu Ala	
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Cys Thr Lys Ser Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Phe Tyr	
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Gly Asp Leu Val Asn Tyr Leu His Lys Asn Arg Asp Ser Phe Leu Ser	
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His His Pro Glu Lys Pro Lys Lys Glu Leu Asp Ile Phe Gly Leu Asn	
700 705 710	

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Pro Met Leu Glu Arg Lys Glu Val Ser Lys Tyr Ser Asp Ile Gln Arg		
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Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
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Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
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Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
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Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
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Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
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Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
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Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Ser Ala Ile Ile Pro Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
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Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
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Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
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Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
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Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
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Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
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Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
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Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
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Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
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Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
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Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
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Val Glu Val Arg Ala Tyr Pro Pro Arg Ile Ser Trp Leu Lys Asn
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Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
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Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
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Lys Glu Glu Asp Ser His Tyr Thr Ile Val Ala Gln Asn Asp
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Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
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Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
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Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
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Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
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Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
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Asp Ile Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp
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Ala Val Lys Met Leu  Pro Thr Ala Arg Ser Ser Glu Lys  Ala
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Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
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Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
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Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
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Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
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Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
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Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
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Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
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Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
 820 825 830

Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
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Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
 850 855 860

Glu Ser Ile Phe Asp  Leu Tyr Thr Thr Leu Ser Asp Val  Ser
865 870 875 880

Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
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Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
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Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
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Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
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His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
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Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
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Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
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Tyr Lys Asn Glu Glu Asp Lys Leu Lys Asp Trp Glu Gly Gly Leu Asp
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 Ser Trp Gln Tyr Pro Met Ser Glu Glu Glu Ser Ser Asp Val Glu Ile
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 Ser Ser Ala Ser Ala Ala His Thr Gly Leu Tyr Thr Cys Tyr Tyr Asn
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 His Thr Gln Thr Glu Glu Asn Glu Leu Glu Gly Arg His Ile Tyr Ile
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 Tyr Val Pro Asp Pro Asp Val Ala Phe Val Pro Leu Gly Met Thr Asp
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Asn	Leu	His	Glu	Val	Lys	His	Phe	Val	Val	Glu	Val	Arg	Ala	Tyr	Pro
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Arg	Ser	Lys	Leu	Lys	Ile	Arg	Ala	Lys	Glu	Glu	Asp	Ser	Gly	His		
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Cys	Asn	Asn	Glu	Thr	Ser	Trp	Thr	Ile	Leu	Ala	Asn	Asn	Val	Ser	Asn	
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Pro	Ile	Tyr	Ile	Ile	Thr	Glu	Tyr	Cys	Phe	Tyr	Gly	Asp	Leu	Val	Asn	
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Gly	Lys	Ile	Val	Lys	Ile	Cys	Asp	Phe	Gly	Leu	Ala	Arg	Asp	Ile	Met	
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cat	gat	tcg	aac	tat	gtg	tcg	aaa	ggc	agt	acc	ttt	ctg	ccc	gtg	aag	2959
His	Asp	Ser	Asn	Tyr	Val	Ser	Lys	Gly	Ser	Thr	Phe	Leu	Pro	Val	Lys	
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Gly Thr Pro Tyr Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys		
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Ile Lys Ser Gly Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu		
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Val Tyr Glu Ile Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg		
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Pro Ser Phe Tyr His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly		
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Gly Lys Arg Asn Arg His Ser Ser Gln Thr Ser Glu Glu Ser Ala		
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Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
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Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
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Val Glu Val Arg Ala Tyr Pro Pro Arg Ile Ser Trp Leu Lys Asn
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775

780

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1015

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His His Pro Glu Lys Pro Lys Lys Glu Leu Asp Ile Phe Gly Leu Asn	
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Pro Ala Asp Glu Ser Thr Arg Ser Tyr Val Ile Leu Ser Phe Glu Asn	
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Pro Met Leu Glu Arg Lys Glu Val Ser Lys Tyr Ser Asp Ile Gln Arg	
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Ser Leu Tyr Asp Arg Pro Ala Ser Tyr Lys Lys Lys Ser Met Leu Asp	

760

770

775

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Phe Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn	
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Val Leu Leu Ala Gln Gly Lys Ile Val Lys Ile Cys Asp Phe Gly Leu	
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Ile Phe Ser Leu Gly Gly Thr Pro Tyr Pro Gly Met Met Val Asp Ser	
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Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
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Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
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Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
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Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
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Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
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Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
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Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
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Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
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Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
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Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
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Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
850 855 860

Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
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Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
885 890 895

Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
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Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
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Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
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His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
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Lys Pro Arg Tyr Glu Ile Arg Trp Xaa Xaa Xaa Xaa Xaa Ile Xaa Xaa	
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Xaa Xaa Xaa Xaa Tyr Ile Tyr Val Asp Pro Met Gln Leu Pro Tyr Asp	
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Gly Ser Gly Ala Phe Gly Lys Val Val Glu Gly Thr Ala Tyr Gly Leu	
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Ser Arg Ser Gln Pro Val Met Lys Val Ala Val Lys Met Leu Lys Pro	
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Thr Ala Arg Ser Ser Glu Lys Gln Ala Leu Met Ser Glu Leu Lys Ile	
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Met Thr His Leu Gly Pro His Leu Asn Ile Val Asn Leu Leu Gly Ala	
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Cys Thr Lys Ser Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Phe Tyr	
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His His Pro Glu Lys Pro Lys Lys Glu Leu Asp Ile Phe Gly Leu Asn	
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Pro Ala Asp Glu Ser Thr Arg Ser Tyr Val Ile Leu Ser Phe Glu Asn	
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Pro Met Leu Glu Arg Lys Glu Val Ser Lys Tyr Ser Asp Ile Gln Arg	
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Ser Leu Tyr Asp Arg Pro Ala Ser Tyr Lys Lys Lys Ser Met Leu Asp	
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Ser Glu Val Lys Asn Leu Leu Ser Asp Asp Asn Ser Glu Gly Leu Thr	
780 785 790	
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Leu Leu Asp Leu Leu Ser Phe Thr Tyr Gln Val Ala Arg Gly Met Glu	
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Phe Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn	
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<223> The 'Xaa' at location 560 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp,

Cys, or Phe.

<220>
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<223> The 'Xaa' at location 561 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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<223> The 'Xaa' at location 564 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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<223> The 'Xaa' at location 566 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

<220>
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<223> The 'Xaa' at location 567 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

<220>
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<223> The 'Xaa' at location 568 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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<222> (569)..(569)
<223> The 'Xaa' at location 569 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

<220>
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<222> (570)..(570)
 <223> The 'Xaa' at location 570 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <222> (571)..(571)
 <223> The 'Xaa' at location 571 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <222> (841)..(841)
 <223> The 'Xaa' at location 841 stands for Lys, Arg, Thr, or Ile.

<220>
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 <222> (842)..(842)
 <223> The 'Xaa' at location 842 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <223> The 'Xaa' at location 843 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <223> The 'Xaa' at location 844 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <223> The 'Xaa' at location 846 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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 <223> The 'Xaa' at location 847 stands for Lys, Asn, Arg, Ser, Thr, Ile, Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, Tyr, Trp, Cys, or Phe.

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Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
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Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
 65 70 75 80

Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
 85 90 95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
 100 105 110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
 115 120 125

Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
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Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
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Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
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Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
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Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
 195 200 205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val

210

215

220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
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Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
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Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
 260 265 270

Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
 275 280 285

Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
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Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
 305 310 315 320

Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
 325 330 335

Val Glu Val Arg Ala Tyr Pro Pro Arg Ile Ser Trp Leu Lys Asn
 340 345 350

Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
 355 360 365

Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
 370 375 380

Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
 385 390 395 400

Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
 405 410 415

Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
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Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
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Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile

450

455

460

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Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
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Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
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Ala Ala Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val
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Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly
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Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
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Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
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Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
 645 650 655

Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
 660 665 670

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690

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700

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Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
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Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
740 745 750

Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
755 760 765

Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
770 775 780

Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
785 790 795 800

Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
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Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
820 825 830

Lys Ile Cys Asp Phe Gly Leu Ala Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
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Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr

930

935

940

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